

AMENDMENTS
(Amendments under Article 11)

To the Commissioner of Patents

1. Identity of the International Patent
PCT/JP02/11747

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4. Subject of Amendments
Specification and Claims

5. Contents of Amendments
As those in the attachments enclosed herewith

6. Attachments

- | | |
|---|---|
| (1) New pages 3, 4, and 13 of Specification | 1 |
| (2) New page 14 of Claims | 1 |
- (The pages 3, 4 and 13 of Japanese specification correspond to pages 3, 4, 13 and 14 of English specification. The page 14 of Japanese specification corresponds to page 15 of English specification.)

The amendments were received by JPO on May 7, 2003.

A. Explanations of the contents of amendments of specification

- (1) The recitation on page 3, line 9 of the specification (written in Japanese) is amended to include “the external medicine which dissolves” after “in an aqueous solution”.
- (2) The recitation on page 3, lines 12 and 13, of the specification (written in Japanese) is amended to include “each” after “pectin”.
- (3) The recitation on page 4, lines 5 and 6, of the specification (written in Japanese) is amended to include “each” after “pectin”.
- (4) The recitation on page 13, line 3, of the specification (written in Japanese) is amended to include “a external medicines which dissolves” after “in an aqueous solution”.
- (5) The recitation on page 13, line 5, of the specification (written in Japanese) is amended to include “, and” instead of “, and”.
- (6) The recitation on page 13, line 6, of the specification (written in Japanese) is amended to include “each” after “pectin”.

B. Explanations of the contents of amendments of claims

- (1) The recitation of line 4 of claim 1 (written in Japanese) is amended to include “the external medicine which dissolves” after “in an aqueous solution”.
- (2) The recitation of line 6 of claim 1 (written in Japanese) is amended to include “, and” instead of “, and”.
- (3) The recitation on line 7 of claim 1 (written in Japanese) is amended to include “each” after “pectin”.

Furthermore, by the aforementioned external medicine, it is possible to maintain electrolyte balance and osmotic pressure balance, and to make the medicinal effect of an adrenocortical steroid act effectively. As a result of these features, the curing effects were widely observed from the external medicine on many conditions, such as atopic dermatitis, seborrheic dermatitis, psoriasis vulgaris, eczema, acne and the like. In these conditions that were cured, the seborrheic dermatitis, eczema, acne, and the like were able to show effectiveness rates which showed an average of 96% or more. On the other hand, the atopic dermatitis showed effectiveness rate which was an average of only about 95%, and the psoriasis vulgaris showed effectiveness rate which was an average of only about 90%.

That is, when the aforementioned external medicine for treatment was used, the stable high effect was observed with respect to the seborrheic dermatitis, eczema, the acne and the like, but a variation of the effect was observed in atopic dermatitis, and an inferior result compared with other conditions was observed in psoriasis vulgaris.

The present invention aims to further improve the aforementioned external medicine for treating dermatitis in order to provide an external medicine for treating dermatitis, which has higher curing effect especially for atopic dermatitis and psoriasis vulgaris.

Disclosure of Invention

An external medicines for treating dermatitis wherein an adrenocortical steroid is included by a cyclodextrin; and 0.025 to 0.5% by weight of the adrenocortical steroid, 0.2 to 30% by weight of the cyclodextrin, and 0.5 to 55% by weight of a dextran or a pullulan are dissolved in an aqueous solution containing a polysaccharide, is prepared by the present invention. In this pharmaceutical, 0.5 to 55% by weight of xyloglucan, trehalose, laminaran, krestin, and pectin are blended. At this time, after the adrenocortical steroid is dissolved at room temperature using a homo-mixer to include the adrenocortical steroid in the cyclodextrin, they are added in the aqueous solution while stirring the solution uniformly.

As other ingredients which are added to the aqueous solution, grape sugar,

mutan, lentinan, sodium chloride, and potassium chloride are added into the aqueous solution. By such a solution, the similar environment as those obtained by intercellular substance liquid is made in a cell, and the cell can promote the tendency to perform normal activity. As a result, synergism between the natural curing energy with which
5 the living body itself is provided and the adrenocortical steroid agent can be provided.

Best Mode for Carrying Out the Invention

The basic compounding of a the present invention is that an adrenocortical steroid is dissolved in the aqueous solution containing a polysaccharide wherein the
10 adrenocortical steroid is beforehand included in a cyclodextrin, in order to dissolve the adrenocortical steroid, which has hardness of dissolving in water, in an aqueous solution.

As an adrenocortical steroid, diflorasones, hydrocortisones, methyl predonisolones, dexamethasones, and betamethasones are mainly used. The content of the adrenocortical steroid is 0.025 to 5% by weight based on the entire contents.
15 Moreover, the content of the cyclodextrin which contains the adrenocortical steroid is 0.2 to 40% by weight based on the entire contents.

Furthermore, 0.5 to 55% by weight of xyloglucan, laminaran, krestin, trehalose, and pectin are blended.

Xyloglucan is a component sugar chain which exists universally in the wall
20 (primary wall) of a plant cell which has elongated and hypertrophied. Plant species specificity is produced when galactose or fucosyl-galactose combines with a xylose residue. Lectin can combine with the galactose residue and the fucose residue respectively, but the function of these branch sugar chain is not solved. Growth of a plant cell is provided according to the water absorption phenomenon which is originating
25 in the osmotic pressure which the cell has, and the suction force is produced by reduction of wall pressure which is caused by the slack of a cell wall. Although the slack of the cell wall is not yet solved, cell extension is always performed with solubilization and decomposition of xyloglucan, and xyloglucan is observed as one of the polysaccharides which manage the physiological activity of a cell.

30 Laminaran is one of the carbohydrates and is classified as a laminaran of β

Table 3

Morbidity	Object number	Effectiveness	Effective rate
Atopic dermatitis (1)	25	48	96
Atopic dermatitis (2)	10	19	95
Atopic dermatitis (3)	25	46	92
Atopic dermatitis (4)	25	49	98
Seborrheic dermatitis (1)	25	48	96
Seborrheic dermatitis (2)	100	198	99
Seborrheic dermatitis (3)	10	19	95
Psoriasis vulgaris	5	9	90
Eczema	25	48	96
Acne	50	99	99

Table 3 shows the results of the pharmacological test of the prescription example 7 (the conventional prescription). (The calculation method of effectiveness and the clinic where the pharmacological test was conducted were the same as those of Table 1). As is apparent from the results, the effective rate of atopic dermatitis is only about 95%, and the effective rate of psoriasis vulgaris about an average of 90%, although the conventional prescription provide an average of 96% or more of effective rate with respect to the seborrheic dermatitis, eczema, acne and the like.

On the other hand, it is clear from the prescription example 1 that the cure effect is increased with respect to atopic dermatitis and a psoriasis vulgaris especially, by adding xyloglucan, trehalose, laminaran, krestin, and pectin.

Industrial Applicability

An external medicines for treating dermatitis, wherein an adrenocortical steroid

is included by cyclodextrin, and 0.025 to 0.5% by weight of the adrenocortical steroid, 0.2 to 30% by weight of the cyclodextrin, and 0.5 to 55% by weight of a dextran or a pullulan are dissolved in an aqueous solution containing a polysaccharide, is provided by the present invention, and by including 0.5 to 55% of the weight of xyloglucan, trehalose, 5 laminaran, krestin and pectin in the external medicine, the excellent and stabilized cure effect is achieved even in the atopic dermatitis wherein the variation of an effect have been observed when the previous external medicine is used.

Moreover, even in the psoriasis vulgaris, which showed inferior cure effect compared with other dermatitises when the previous external medicine for treatment was 10 used, the effective rate was able to be raised to the levels of other dermatitis by the present invention.

In this way, according to the present invention, it become possible to greatly raise an effective rate as compared with previous external medicines. Particularly, the external medicine of the present invention is very effective in diseases which have been 15 difficult to cure such as atopic dermatitis, seborrheic dermatitis and the like. From view points such as high cure rate and high safety such as extremely low side effects, the external medicine of the present invention can be used as a medicine which can supersede the conventional external medicine. The external medicine of the present invention can be expected to be used for a large number of patients and the like all over 20 the world who have suffered from intractable dermatitis. The significance of the present invention is great, and it can greatly contribute to human beings.

**REPLACED BY
ART 34 AMDT**

CLAIMS

1. An external medicine for treating dermatitis wherein an adrenocortical steroid is included by a cyclodextrin; and 0.025 to 0.5% by weight of the adrenocortical steroid,
5 0.2 to 30% by weight of the cyclodextrin, and 0.5 to 55% by weight of dextran or pullulan are dissolved in an aqueous solution containing polysaccharide; and 0.5 to 55% by weight of xyloglucan, trehalose, laminaran, krestin, and pectin are blended.
2. An external medicine according claim 1, wherein the aqueous solution containing
10 polysaccharide includes grape sugar, mutan, lentinan, sodium chloride, and potassium chloride.